

### **REMARKS**

Applicants respectfully request the Examiner to reconsider the merits of the objections and rejections in view of the foregoing amendment and following remarks.

Upon entry of the foregoing amendment, claims 57, 58, 63-69, 71, 74, 76, 77, 79-81, 83, 85 and 86 are pending in the Application. New claims 85 and 86 are added. Claims 82 and 84 are cancelled without prejudice to or disclaimer of the subject matter contained therein. Claims 71, 77 and 83 are amended.

Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter.

Support for the amendments to the claims and new claims can be found throughout the specification and in the claims as originally filed. In particular, support for new claim 85 can be found, *inter alia*, in the specification at page 31, line 8 to page 32, line 10 (Example 4). Support for new claim 86 can be found, *inter alia*, in the specification at page 32, lines 1-10 (Example 4). Applicants amend claim 71 solely to expedite prosecution by resolving an informality. Applicants amend claim 77 solely to expedite prosecution by resolving a grammatical issue. Applicants amend claim 83 and cancel claim 84 solely to expedite prosecution by resolving an informality.

Applicants thank the Examiner for indicating that claims 57, 63-69, 74, 79 and 81 are allowed.

Based on the instant amendment and remarks, Applicants respectfully request that the Examiner withdraw the outstanding objections and rejections.

### **I. Objections to the Claims**

#### **A. Claim 71**

The Office Action maintains the objection to claim 71 on the ground that, according to the Office Action, the article "a" before "leader" in part (b) is improper. Applicants traverse this objection; however, solely to expedite prosecution, and without changing the scope of the claim,

claim 71, as amended, does not recite "a" before the term "leader" in part (b). In any case, Applicants respectfully assert that, in view of the differences in choice of restriction sites within the recited leader sequence or for optimal matching to other sequences, it would be readily apparent to one of ordinary skill in the art that different lengths of leader sequence, with some linked oligonucleotides for optimal cloning, for example, are encompassed by claim 71 as amended.

With regard to the phrase "a 3' transcript termination and polyadenylation region which is a DNA sequence from the 3' transcript termination and polyadenylation region of the Cauliflower Mosaic Virus 35S gene" recited in claim 71, Applicants submit with the instant Reply Appendix A containing Sanfaçon, et al., *A Dissection of the Cauliflower Mosaic Virus Polyadenylation Signal*, *Genes & Development* 5:141-149 (1991) (the "Sanfaçon reference"). The Sanfaçon reference demonstrates that, at the time of filing of the instant Application, it was recognized in the art that variation can be present in a polyadenylation site from the Cauliflower Mosaic virus while still achieving 3' end formation. Therefore, the article "a" before "3' transcript termination and polyadenylation region" is proper, as claim 71 encompasses at least several 3' end regions and variations derived from the 35S gene of the Cauliflower Mosaic virus.

Accordingly, Applicants respectfully request that the Examiner withdraw the objection to claim 71.

#### **B. Claims 82 and 84**

The Office Action objects to claims 82 and 84 on the ground that claims 82 and 84 are allegedly in improper dependent form. Applicants are canceling claims 82 and 84 solely to expedite prosecution and without acquiescing to the objections to claims 82 and 84. Thus, the objections to claims 82 and 84 have been rendered moot, and Applicants request the Examiner to withdraw these objections.

#### **II. Rejection under 35 C.F.R. § 112, para. 2**

Applicants thank the Examiner for withdrawing the rejections of claims 64, 66-68, 71-76 and 78 under 35 U.S.C. § 112, para. 2.

The Office Action maintains the rejection of claim 77 under § 112, para. 2, on the ground that “[i]t is suggested that ‘said’ be replaced with --the truncated insecticidal Cry2Ae--.” (Office Action, page 4.) Applicants are amending claim 77 in accordance with the Examiner’s suggestion solely to expedite prosecution and without changing the scope of the claim or acquiescing to the rejection of claim 77 under § 112, para. 2. Therefore, the rejection of claim 77 is rendered moot.

### **III. Rejection under 35 U.S.C. § 102(e)**

The Office Action rejects claims 83 and 84 under 35 U.S.C. § 102(e) as anticipated by the U.S. Patent No. 6,593,293, issued to Baum et al. (the “Baum ‘293 patent”). The Office Action states that “Baum et al teach a method comprising apply the protein of SEQ ID NO:2 (claims 9-10; column 50, line 25, to column 55, line 15).” (Office Action, page 5.) Applicants respectfully traverse this rejection. However, as discussed above, Applicants are canceling claim 84 to expedite prosecution by resolving an informality, and claim 83 is amended to reflect the subject matter of previous claim 84.

Applicants submit that claim 83, as amended, is not anticipated under § 102(e) by the Baum ‘293 patent. Anticipation can be established only by a single reference that discloses each and every element of the claimed invention. *See Structural Rubber Prods. Co. v. Park Rubber Co.*, 749 F.2d 707, 716, 223 U.S.P.Q. 1264, 1270 (Fed. Cir. 1984); M.P.E.P. § 2131 at 2100-73 (8th ed., Rev. No. 2). If a single element required by the claim is missing in the reference, there can be no anticipation. *See Structural Rubber*, 749 F.2d at 707, 223 U.S.P.Q. at 1271-72.

The Baum ‘293 patent does not disclose each and every feature of amended claim 83. In particular, the Baum ‘293 patent does not disclose anywhere in its text, including the Examiner-cited portion (claims 9-10; col. 50, line 25 to col. 55, line 15), a method for protecting a plant of interest from *Anticarsia gemmatalis* insects, comprising applying the polypeptide of SEQ ID NO: 2 or a transformed cell comprising a polynucleotide sequence encoding the polypeptide of SEQ ID NO: 2. As the Baum ‘293 patent does not contain each and every feature of claim 83, the Baum ‘293 patent cannot anticipate claim 83. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of claim 83 under § 102(e).

Moreover, Applicants submit that claim 83 is non-obvious. For example, according to the Baum '293 patent, the Baum '293 patent shows that certain Bt crystal proteins are toxic to some insects but not toxic to others. It is well known in the art that these crystal proteins have a limited range of target insects, and therefore it would furthermore not be possible to predict whether any particular protein, such as the one claimed, would be toxic to *Anticarsia gemmatalis* from the cited art.

Accordingly, as claim 83 is both novel and non-obvious, Applicants respectfully submit that claim 83 is in condition for allowance.

#### **IV. Rejection under 35 U.S.C. § 103(a)**

Applicants thank the Examiner for finding that claims 57, 63-69, 74 and 81-82 are free of any prior art. Applicants furthermore thank the Examiner for withdrawing certain of the rejections of claims 57-58, 63-71, 74, 76-77 and 79-82 under 35 U.S.C. § 103(a).

##### **A. Claims 58, 77 and 80**

According to the Office Action, claims 58, 77 and 80 are rejected under § 103(a) as purportedly unpatentable over the Baum '293 patent in view of Audtho, et al., *Product of Chymotrypsin-Resistant Bacillus thuringiensis Cry2Aa1  $\delta$ -Endotoxin by Protein Engineering*, Applied & Environ. Microbiol. 65:4601-4605 (October 1999) (the "Audtho reference") and further in view of Schnepf, et al., *Bacillus thuringiensis and its Pesticidal Crystal Proteins*, 62 Microbio. & Mol. Bio. Revs., 775-806 (September 1988) (the "Schnepf reference").

As a preliminary matter, Applicants respectfully disagree with the statement that "the claims are drawn to a nucleic acid encoding a protein consisting of amino acids 2-49 to 632 of SEQ ID NO:2 or a protein of SEQ ID NO: 2 . . . ." (Office Action, page 5.) Such a statement does not accurately characterize Applicants' invention encompassed by claims 58, 77 and 80 because claims 58, 77 and 80 are directed to the recited truncated proteins.

The Office Action states that

Audtho et al teach that another Cry2 protein, Cry2Aa1, is activated by processing at the N-terminal end . . . . .

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the nucleic acids taught by Baum et al., to remove about 49 amino acids from the N-terminus of the protein, as described in Audtho et al. One of ordinary skill in the art would have been motivated to do so because truncation of the modified Cry genes results in more effective expression in plants (Schnepf . . . ) and to avoid insect resistance (Schnepf . . . ).

(Office Action , page 6.) Applicants respectfully traverse this rejection.

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the reference or to combine reference teachings. MPEP § 2143, 2100-135 (8<sup>th</sup> ed., rev. no. 3).

Applicants respectfully assert that the prior art does not provide any motivation to combine the reference teachings cited by the Examiner because the prior art does not teach or suggest the desirability of Applicants' invention. Applicants' invention encompassed by claims 57, 77 and 80 involve truncated Cry2Ae proteins. The protein disclosed in the Audtho reference is not Cry2Ae; rather the Audtho reference discloses a Cry2Aa protein. Although the Office Action combines the Audtho reference's disclosure of proteolytic cleavage of a Cry2Aa protein resulting in a particular N-terminal protein fragment with the disclosure of a full-length Cry2Ae protein in the Baum '293 patent, the Examiner does not set forth any objective reason why a skilled artisan would be motivated to combine such disclosures to form Applicants' isolated DNA sequence encoding an insecticidal Cry2Ae protein truncated at the N-terminus.

Specifically, the Office Action does not explain why one of skilled in the art would be motivated to apply teachings relating to one protein to a teachings relating to a different protein. As Applicants' specification shows in Table IV, page 31, there is about a 10% difference in sequence between the Cry2Ae protein and the Cry2Aa protein. Such different types of Cry2A proteins were *not* known to be substitutable.

Indeed, U.S. Patent No. 6,489,542, issued to Corbin et al. (the "Corbin '542 patent"), which was cited by the Examiner in the Office Action of February 24, 2004, demonstrates that different Cry2A protein types act in a completely different manner when expressed in plants. Regarding the Cry2Aa protein type and the Cry2Ab protein type, the Corbin '542 patent states: "As disclosed herein, localization of Cry2Aa to the chloroplast or plastid results in decreased

levels of expression as measured by accumulation of Cry2Aa delta-endotoxin, which is in contrast to the improved expression of chloroplast or plastid localized Cry2Ab delta-endotoxin.” (Corbin ‘542 patent, col. 19, lines 43-74.) The Corbin ‘542 patent also demonstrates in Examples 5 and 6 that Cry2Aa protein expression in plants leads to “significantly” decreased expression and abnormal plant phenotypes when using a targeting signal. (Corbin ‘542 patent, col. 49, line 11-13.) This is in contrast to the Cry2Ab protein, which, when expressed with a transit peptide, allowed high expression without such negative results (*see* Examples 1-4). Applicants’ specification shows in Table IV that these two types of Cry2A proteins also differ in their amino acid sequences by about 10%.

Thus, the Corbin patent establishes that it was known in the art that different types of full-length Cry2A proteins, which differ in their amino acid sequence by about 10%, cannot be substituted one for another. As there are major differences between different types of Cry2A proteins, no motivation existed to combine a disclosure relating to digestion of one Cry2A protein type to a disclosure relating to the full-length sequence of another Cry2A protein type, especially in the context of expression of Cry2A proteins in plants.

The Examiner-cited portions of the Schnepf reference do not provide the requisite motivation to combine the Baum ‘293 patent with the Audtho reference. The Examiner-cited portions of the Schnepf reference do not even involve Cry2A proteins. Importantly, the citation to the Schnepf reference on page 793 is a reference to the Barton, Fischhoff and Vaeck papers involving Cry1Aa and Cry1Ab proteins, which were truncated from a DNA encoding a 130 kD protein in nature to a protein encoding a protein about 65-70 kD in plants, by removing a C-terminal part of the protein (removal of 3’ part of the gene). The Examiner-cited portions of the Schnepf reference do not even address Cry2A proteins and thus certainly do not suggest whether or not truncation for a Cry2A protein (having a molecular weight of about 65-70 kD in nature) would be beneficial for expression in plants.

Moreover, the citation to the Schnepf reference on page 795, which merely states “[g]iven multiple steps in processing the crystal to an active toxin . . . , it is not surprising that insect populations might develop various means of resisting intoxication,” provides no motivation to the skilled artisan that truncating a specific Cry protein would be beneficial to prevent insect resistance, and especially not with regard to Cry2A proteins, which are already of

the size of a truncated CryIA protein. Therefore, it certainly does not teach or suggest the desirability of Applicants' inventive concept involving isolated DNA sequence encoding a truncated insecticidal Cry2Ae protein.

Overall, then, as no motivation existed in the art to form Applicants' inventive concept relating to DNA sequences encoding the recited truncated Cry2Ae proteins, the Office Action does not fulfill the requirements for a *prima facie* case of obviousness. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of claims 58, 77 and 80 under § 103(a).

#### **B. Claims 71 and 76**

The Office Action rejects claims 71 and 76 as purportedly obvious under 35 U.S.C. § 103(a). Applicants traverse this rejection. Solely to expedite prosecution, Applicants are amending claim 71 to depend from claims 57 or 58.

As discussed above, claim 58 is novel and non-obvious over prior art. As claims 71 and 76 depend directly or indirectly from claim 57, which the Office Action indicated is free of prior art, or claim 58, claims 71 and 76 are likewise novel and non-obvious.

Therefore, Applicants respectfully request the Examiner to withdraw the rejection of claims 71 and 76 under § 103(a).

**CONCLUSION**

Applicants respectfully request entry of the above claim amendments.

All of the stated grounds of objection and rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

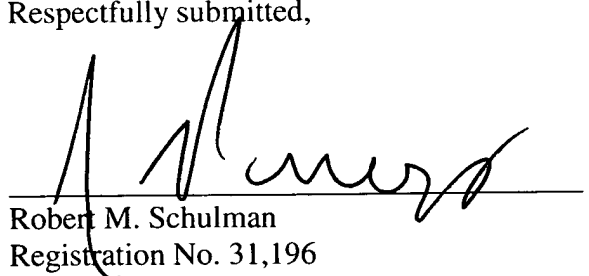
The Examiner is respectfully requested to contact the undersigned by telephone at the below listed telephone number, in order to expedite resolution of any issues and to expedite passage of the present application to issue, if any comments, questions, or suggestions arise in connection with the present application.

In view of the above claim amendments and remarks, early notification of a favorable consideration is respectfully requested. A check in the amount of \$1,020.00 is enclosed to cover the three-month extension of time fee. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account Number 50-0206.

Respectfully submitted,

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